II. The rejection under 35 U.S.C. §112, first paragraph should be withdrawn.

Claim 1 has been rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one of skill in the relevant art that the inventors had possession of the claimed invention. In support of the rejection, the examiner stated that "while the specification as originally filed teaches both the enzymatic test kit and the nucleic acid sequences set forth in the claim, the specification does not disclose a diagnostic kit comprising both of these components . . . ." Official action at 3. In response, the applicants traverse the rejection.

The present invention describes a kit for the diagnosis of tuberculosis and other mycobacterial infections in humans or animals. Referring to page 31, line 15, through page 32, line 8 of the specification, it can be seen that deletion of base 272 in the alaDH gene results in a lack of AlaDH enzyme activity. At page 33, the specification teaches that "a slow-growing mycobacterium having positive AlaDH activity is virulent. The converse of that statement, is however, false. Among the strains that do not have AlaDH activity, several are virulent." Thus, the specification teaches that while AlaDH enzyme activity correlates with virulence of mycobacteria the absence of AlaDH activity does not correlate with avirulence. Thus, in order to determine the virulence of a mycobacterium, one of skill in the art must determine both the AlaDH enzyme activity ***and*** determine whether AlaDH DNA is present in the mycobacterium.

Claim 1 as amended recites a diagnostic kit preamble, followed by the open-ended transitional term "comprising," in turn followed by the body of the claim, which provides the two features identified by the examiner - the enzymatic test kit and the nucleic acid sequences. The examiner acknowledges that the application as filed provides written descriptive support for both features found in the body of the claim, but asserts that the combination of an enzymatic test kit and nucleic acid sequences is not disclosed. As previously noted by the applicants, however, the application as filed recites that "[t]he disclosure also includes all conceivable combinations of the individual features disclosed." Specification, page 37, lines 6-7. Thus, one of skill would recognize that the applicants were in possession of the combination of features recited in pending claim 1.

The examiner also supported the rejection by noting that "the specification does disclose not a method in which the claimed combination of components is employed. Accordingly, the specification does not provide basis for the diagnostic kit of claim 1." Official action at 3. In response, the applicants again cite original claim 14, which recites: "[a] method according to claim 2 and/or 10, characterised in that a clinical sample is used directly and diagnosed for tuberculosis in humans and animals." Investigating the conjunctive version of this claim, and substituting the language of claims 2 and 10 for the references thereto contained in claim 14, the subject matter of claim 14 becomes:

> [a] method for the diagnosis of tuberculosis and other mycobacterial infections of humans and animals, characterised in that the activity of alanine dehydrogenase (E.C. 1.4.1.1.) is measured with an enzymatic test kit according to claim 1 and the use of a DNA sequence according to claim 9 for the diagnosis of tuberculosis and other mycobacterial infections in humans and animals, characterised in that a clinical sample is used directly and diagnosed for tuberculosis in humans and animals.

Thus, the examiner's unsupported assertion that the specification does not disclose a method in which the claimed combination of components is employed is contradicted by original claim 14, which is part of the specification for purposes of assessing satisfaction of 35 U.S.C. § 112 requirements. In fact, the evidence cited above, and evidence cited in the applicants' prior responses, establishes that the application as filed most certainly disclosed a method in which the claimed combination of components is employed. Thus, the examiner's premise is flawed in that the application as filed did disclose a method in which the claimed combination of components is employed. Accordingly, it does ***not*** follow that the specification does not provide basis for the diagnostic kit of claim 1. Rather, by the examiner's own reasoning, because there is incontrovertible support for the corresponding method in which the combination of components is employed, it follows that there ***is*** basis for the diagnostic kit of claim 1 in the application as filed.

Moreover, the supportive description(s) in the application as filed that are addressed above and in applicants' prior responses, coupled with the examiner's acknowledgment noted above, establish that the features recited in the body of claim 1 are supported in the application as filed. Therefore, any written descriptive issue that might remain has been narrowed to the recitation of a "diagnostic kit" in the preamble

of claim 1. The applicants submit that the body of claim 1 provides a complete definition of the claimed subject matter and the preamble of that claim is not necessary to understand the claim as a whole. The Federal Circuit has established that "where a patentee defines a structurally complete invention in the claim body and uses the preamble only to state a purpose or intended use for the invention, the preamble is not a claim limitation." *Rowe v. Dror*, 112 F.3d 473, 42 U.S.P.Q.2d 1550, 1553 (Fed. Cir. 1997). As such, applicants submit that the diagnostic kit of claim 1 is fully supported by the description as filed, regardless of whether or not there is an *ipsis verbis* recitation of such a kit in the specification.

Notwithstanding the applicants' position that pending claim 1 is supported by a sufficient written description, to move prosecution forward, the applicants solicit the examiner's suggestions for terms of equivalent nature and scope to be used in place of the existing non-limiting terms found in the preamble of that claim.

III. The rejection under 35 U.S.C. §112, second paragraph, should be withdrawn.

Claim 1 was rejected under 35 U.S.C. §112, second paragraph, as being indefinite for reciting "hybridizable therewith." In particular, the examiner inquired whether this phrase was intended to limit the subject matter to nucleic acids that actually hybridized or to nucleic acids that would have the potential to hybridize if particular reagents, etc., were present. In response, the applicants clarify that the claim phrase "hybridizable therewith" is used consistently with its ordinary and accustomed meaning, *i.e.*, that the nucleic acids would have the potential to hybridize if the conditions recited in the claim were present. In this manner, the applicants have claimed kits containing nucleic acids that are structurally defined by their hybridization behavior with a reference nucleic acid of specified sequence under specified conditions. The pending claim is drawn to a kit that is structurally defined and is not defined by any process of use. The applicants respectfully submit that the phrase "hybridizable therewith" is definite in that one of skill would understand it to mean that the nucleic acids have the potential to hybridize under certain conditions, rather than requiring that they actually hybridize, and applicants' use of the phrase is consistent with that meaning. Accordingly, the rejection has been overcome and should be withdrawn.

IV. The rejection under 35 U.S.C. §103 should be withdrawn.

The examiner rejected claim 1 under 35 U.S.C. §103(a) as allegedly obvious over Andersen et al. ("Andersen"), in view of Ahern, The Scientist 9:20 (1995) ("Ahern") and optionally in view of Innis et al., *in* PCR Protocols: A Guide to Methods and Applications, (Innis, et al. eds.) Academic Press, Inc., San Diego, 1990 pages 3-12 ("Innis"). In support of the rejection, the examiner asserted that Andersen disclosed a nucleic acid sequence of *alaDH*, as well as methods for characterizing the encoded polypeptide in which all the components (stain or assay components) set forth in the claim are employed. Official action at 4. Further, Andersen assertedly discloses that AlaDH is only expressed in some species of mycobacteria and has "'potential relevance....for virulence and/or protection.'" Official action at 5. Ahern was relied upon as disclosing the general benefits of packaging the stain components in a kit, and suggesting the benefits of packaging the stain components and the nucleic acids in another kit. *Id.* For a disclosure of the general benefit of using PCR to amplify nucleic acid targets, as well as the criteria for efficient PCR primers, reliance was placed on Innis. In response, the applicants traverse the § 103(a) rejection based on Andersen, Ahern and, optionally, Innis.

The examiner relies on Andersen as disclosing all of the features recited in claim 1 as amended, stating that:

> Andersen et al teach the nucleotide sequence . . . which comprises each of the sequences set forth . . . . Accordingly, it is a property of the molecule taught by Andersen et al that it is a nucleic acid consisting of a sequence that is "hybridizable" . . . . Andersen et al further teach that L-alanine dehydrogenase activity may be identified by employing a stain comprising NAD, L-alanine, PMS, and NBT (p. 2318). Accordingly, Andersen et al disclose methods for characterizing L-alanine dehydrogenase in which all the components set forth in claim 1 are employed.

The examiner asserts that Andersen discloses "methods" in which all of the components set forth in claim 1 are employed. The applicants respectfully request that the examiner cite with particularity to the disclosure by Andersen of a single "method" in which all such components are employed. In the event that the examiner has combined the disclosure of distinct methods in summarily characterizing Andersen as disclosing "methods" in which all the claim-recited components are employed, then applicants submit that no motivation to select these particular methods from Andersen

has been identified. Accordingly, the applicants submit that the examiner is impermissibly picking and choosing from the Andersen disclosure, using the applicants' specification as a guide to impermissibly arrive at this hindsight reconstruction of the claimed subject matter. The mere fact that a reference ***can*** be modified is not sufficient to establish a *prima facie* case of obviousness. *In re Mills*, 16 USPQ2d 1430 (Fed. Cir. 1990) (*see* MPEP 2143.01).

In addition, applicants submit that Andersen's apparent disclosure of the *alaDH* nucleotide sequence and a set of components for staining its gene product cannot be combined to arrive at the subject matter of claim 1. Andersen did not disclose a nucleic acid consisting of one of the ***expressly provided partial*** sequences of *M. tuberculosis alaDH* for use in conjunction with components used to stain AlaDH. Even if Andersen had disclosed nucleic acids consisting of such partial sequences, there would be no logical reason to combine such nucleic acids with components designed to detect an activity of the AlaDH protein encoded by the full-length gene. Accordingly, the applicants submit that Andersen does ***not*** disclose the claim-recited nucleic acids and each component of the claim-recited enzyme test kit for use in any single method for characterizing AlaDH in mycobacteria.

The defect in the Andersen disclosure is not remedied by either Ahern or Innis. For these reasons, the applicants submit that the rejection of claim 1 under 35 U.S.C. § 103(a) over Andersen in view of Ahern, and optionally in further view of Innis, has been overcome and should be withdrawn.

CONCLUSION

Claim 1 is believed to be allowable in view of the above remarks and an early notice thereof is respectfully solicited.

Respectfully submitted,

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